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Design, optimization and evaluation of ibuprofen fast dissolving tablets employing starch succinate: A new superdisintegrant

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ABSTRACT

The current scenario emphasize on oral administration. The main disadvantage in oral administration was difficulty in swallowing for pediatric and geriatric patients. To solve this problem in oral drug delivery system, the formulation of fast dissolving systems found to be the best alternatives. The present investigation involves in the evaluation of starch succinate as a superdintegrant in the formulation of fast dissolving tablets of poorly soluble drugs employing 2^3factorial design. Starch succinate was synthesized by esterification process. The synthesized starch succinate was subjected to physical and micromeritic evaluation. All fast dissolving tablets were evaluated for drug content, hardness, friability, disintegration time and other dissolution characteristics like percent dissolved in 5 min (PD_5), dissolution efficiency in 5 min (DE_5%) and first order rate constant(K_1). The starch succinate prepared was found to be fine, free flowing crystalline powder. Starch succinate exhibited good swelling in water. Fourier transform infrared spectra (FTIR) and Differential scanning calorimetry (DSC) study indicated the absence of interaction between ibuprofen and starch succinate. All the fast dissolving tablets formulated employing starch succinate were of good quality with regard to drug content (200±2%), hardness (3.6–4.0 kg/sq. cm), and friability (0.12-0.15%). The optimised formulation F8 has the least disintegration time i.e., 15±0. 02s. The *in–vitro* wetting time was less (i.e., 15s) in optimized formulation F8. The water absorption ratio of the formulated tablets was found to be in the range of 31.4±0.01 to 68.0±0.04%. The cumulative drug dissolved in the optimized formulation F8 was found to be 99.81± 0.22% in 5 min. Starch succinate was found to be a superdisintegrant which enhanced the dissolution efficiency with the ibuprofen and hence it could be used in the formulation of fast dissolving tablets to bring immediate release of the contained drug within 5 minutes.

Keywords: Fast dissolving, Superdisintegrant, Starch succinate, Dissolution efficiency.

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INTRODUCTION

Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS has made a significant contribution to global pharmaceutical sales through market segmentation and are moving rapidly. Fast dissolving tablets (FDT) are oral solid dosage forms that disintegrate fastly and release the drug[1] Fast dissolving tablets are also known, “Orally disintegrating tablets”, “Melt-in-mouth”, “Fast dissolving drug delivery”, “Rapimelts tablets”, “Porous tablets”, “Quick dissolving tablets”[2] etc. Recently FDT terminology has been approved by United States Pharmacopoeia, British Pharmacopoeia.[3,6] And Centre for Drug Evaluation and Research (CDER), US FDA defined FDT tablets as “A solid dosage form containing medicinal substances which disintegrates rapidly usually a matter of seconds, when placed upon the tongue”, European pharmacopoeia also adopted the term “orodispersible tablet” as a tablet that is to be placed in the mouth where it disperses, rapidly before swallowing despite various terminologies used[1] Recently, FDT have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better patient compliance especially in elderly and children. In order to allow fast dissolving tablets to dissolve in the mouth, they are made of either very porous and soft-moulded matrices or compressed into tablets with very low compression force, which makes the tablets friable and or brittle, which are difficult to handle, often requiring specialized peel-off blister packaging.

The present investigation deals with an attempt of systematic formulation approach for optimization of ibuprofen fast dissolving tablets employing starch tartrate, crospovidone, and croscarmellose sodium as superdisintegrants. A 2^3 factorial design was applied to investigation the main and interaction effects of the three formulation variables i.e., starch succinate (A), crospovidone (B), croscarmellose sodium (C) in each case to find the

formula with less disintegration time and more dissolution efficiency in 5 min and to authorize the arbitrary selection of tablets with immediate release of drug within 5 min.

MATERIALS AND METHODS

Materials:

Sodium hydroxide, Succinic acid, Mannitol was purchased from Finar chemicals Ltd, Ahmedabad. Potato starch, ibuprofen, crospovidone, croscarmellose sodium was obtained from Yarrow Chem. Products, Mumbai. Microcrystalline cellulose was bought from qualigens fine chemicals, Mumbai. Talc and magnesium stearate was obtained from molychem, Mumbai.

Preparation of starch succinate (a novel superdisintegrant):

Initially succinic acid was dissolved in distilled water and the pH is adjusted to 3.5 using 10M NaOH and finally made up to 50ml. To this potato starch was added and conditioned for 16 hrs, the product was kept in oven at 60ºC for 1hr. Then the product was washed with water to remove any unreacted succinic acid if present. After washing, the resultant starch succinate was kept in oven for 60ºC until it gets dried. The product obtained was ground and dried.

Characterization of starch succinate:

The starch succinate prepared was evaluated for the following

Solubility:

Solubility of starch succinate was tested in water, aqueous buffers of pH 7.2 phosphate buffer.

pH:

The pH of 1% w/v slurry was determined by pH meter.

Melting point:

The melting point was measured by using melting point apparatus.

Viscosity:

The viscosity of 1% dispersion in water was calculated using ostwald viscometer.

Swelling index:

The starch succinate (200 mg) was added to 10 ml of water and light liquid paraffin, taken in two different graduated test tubes and mixed. Then for 12 h the dispersion in the tubes was allowed to stand. The volumes of the sediment in the tubes were noted. The swelling index of the material was determined as follows.

$$S.I(\%) = \frac{\text{Volume of sediment in water} - \text{Volume of sediment in light liquid paraffin}}{\text{Volume of sediment in light liquid paraffin}} \text{ X } 100$$

Test for gelling property:

The gelling property (gelatinization) of the starch and starch succinate prepared was evaluated by heating 7% w/v dispersion of each, in water at 100^{0}C for 30 min.

Particle size:

The particle size analysis was performed by sieving using standard sieves.

Density:

The density (g/cc) was calculated by liquid displacement method using benzene as liquid.

Bulk density:

Both loose bulk density (LBD) and tapped bulk density (TBD) were measured by transferring the accurate weigh amount of sample in 50 ml measuring cylinder, the granules without any agglomerates and calculated the volume of packing and tapped 50 times on a plane surface and tapped volume of packing recorded LBD and TBD calculated by following formula [8].

$$\text{LBD} = \frac{\text{Mass of powder}}{Volume of packing}$$

$$\text{TBD} = \frac{\text{Mass of powder}}{Tapped volume of packing}$$

Percentage compressibility index

The percentage compressibility of powder mix was calculated by Carr's compressibility index calculated by the following formula [9].

$$\%\ \text{Carr's Index} = \frac{(\text{TBD} - \text{LBD})}{\text{TBD}} \text{ X } 100$$

Where, TBD= Tapped bulk density; LBD= Loose bulk density.

Angle of repose

The frictional forces in loose powder or granules can be calculated by the angle of repose. This is the utmost angle possible between the surface of a mass of powder or granules and the horizontal plane. Angle of repose is determined by applying the next equation;

$$\tan\theta = \frac{h}{r} \quad \theta = \tan^{-1}\frac{h}{r}$$

Where θ=angle of repose; h=height of pile; r=radius of pile.

Fourier transform infrared (FTIR) spectroscopy:

FTIR spectra of starch succinate was recorded on samples prepared in potassium bromide (KBr) disks using a BRUKER FT –IR, (Tokyo, Japan). At a hydrostatic press of 6-8 tons' samples were prepared in (KBr) disks. The scanning range was 500 to 4000 cm^{-1}.

X – ray diffraction:

Diffraction pattern of starch succinate was recorded with an x-ray diffractometer (Analytical spectra's Pvt. Ltd., Singapore). X-ray diffraction was performed at room temperature (30^{0}C) with a diffractometer; target, Cu (λ1.54 A), filter, Ni; voltage,40 kV; current 30mA; time constant 10mm/s; scanning rate 2^0/min; calculated from 2.5-50^0 at full scale 200.

Ester test:

To 1mg of starch succinate, 2ml of ethanol and 1ml of 0.1M NaoH was added. To this, phenolphthalein indicator was added. The colour change was observed.

Drug – excipients compatibility studies:

The compatibility of starch succinate with the selected drug (ibuprofen) was evaluated in DSC, FTIR studies and TLC studies.

Differential scanning calorimetry (DSC):

DSC thermograms of ibuprofen and their mixtures (1: 1) with starch succinate were recorded on Perkin Elmer thermal analyser samples (2- 5 mg) were sealed into

aluminium pans and scanned at a heating rate of 10^0C min^{-1} over a temperature range 30 – 350^0C.

Infrared spectroscopy:

Fourier transform infra-red (FTIR) spectra of ibuprofen, and their mixtures (1: 1) with starch succinate were recorded on a Perkin Elmer, IR Spectrophotometer model: Spectrum RXI, using KBr disc as reference.

TLC study:

TLC was carried out on ibuprofen and their mixtures (1:1) with starch succinate follows;

Stationary phase: Silica gel G (pre coated TLC plates).

Mobile phase: n-Hexane, Ethyl acetate, Glacial acetic acid (75:25:5).

Procedure:

Mobile phase was prepared and taken in a TLC chamber. The chamber was allowed to saturate with solvent vapour for 24h. Standard (pure drug) and test (drug-starch succinate mixtures). Samples were spotted on activated silica plates using narrow capillary tubes. The spotted plates were kept in the TLC chamber and allowed to run the mobile phase. The plates were dried and kept in iodine chamber to develop the spots. The R_f values of standard and test samples were determined by the following formula.

R_f = distance travelled by sample / distance travelled by solvent front

Preparation of ibuprofen fast dissolving tablets:

The tablets were prepared by wet granulation method employing 2^3 factorial design in which 3 independent variables {superdisintegrants i.e., starch succinate (A), crospovidone (B), croscarmellose sodium(C)} and 1 dependent variable (dissolution efficiency in 5 min) were selected. The composition of different formulation of ibuprofen fast dissolving tablets is given in table no 1, in which superdisintegrants were selected at 2 levels i.e., higher and lower. At the higher level i.e., 10% concentration of starch succinate (A), crospovidone (B) and croscarmellose sodium(C) and at the lower level i.e., 0% concentration of starch succinate (A), crospovidone (B) and croscarmellose sodium(C).For uniformity in particle size each ingredient was passed through the # 100 mesh sized screen before mixing. Starch succinate, crospovidone, croscarmellose sodium, mannitol and microcrystalline cellulose were accurately weighed and mixed using mortar and pestle, and the added to ibuprofen. Finally, to the powder mixture talc and magnesium stearate were added. Then the mixed blend was compressed by using eight station rotator press Karnawathi Machineries Pvt, Ltd., Ahmedabad, India).

Table: 1: Formulae of ibuprofen fast dissolving tablets employing starch succinate prepared.

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8
Ibuprofen	200	200	200	200	200	200	200	200
Starch succinate	---	50	---	50	---	50	---	50
Croscarmellose sodium	---	---	50	50	---	---	50	50
Crospovidone	---	---	---	---	50	50	50	50
Mannitol	270	220	220	170	220	170	170	220
Potato starch	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10
Magnesium Stearate	10	10	10	10	10	10	10	10
Total weight(mg)	500	500	500	500	500	500	500	500

Evaluation of ibuprofen fast dissolving tablets:

Hardness test

Hardness implies the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Monsanto hardness tester and expressed in kg/cm^2 [10]

Uniformity of weight:

Weight variation test was performed with 20 tablets. It is the individual tablet weight variation from the average weight of 20 tablets.

Friability:

The friability of tablets was determined using a Roche fribilator. At 25 rpm the tablets were rotated for 4 minutes or up to 100 revolutions. After the removal of fines the tablets were reweighed and the percentage of weight loss was determined.

$$F = \frac{100 \text{ X W (initial)} - \text{W (final)}}{\text{W (initial)}}$$

Drug content uniformity:

For drug content uniformity, ten tablets were weighed and powdered a quantity of powder equivalent to 10mg of ibuprofen, which was extracted into 7.2 phosphate buffer and filtered. The ibuprofen content was calculated by measuring the absorbance spectrophotometrically at 221 nm after appropriate dilution with 7.2 phosphate buffer. The drug content was measured as an average of three determinations [11].

Wetting Time:

The wetting time of tablets was determined using a very simple procedure five circular tissue papers of 10 cm diameter were placed in a petri dish with a 10 cm diameter. 10 ml of water containing a water soluble dye (amaranth) was added to the petri dish. A tablet was gently placed on the tissue paper. Time needed for water to reach the upper surface of the tablet was noted as wetting time [12, 13].

Water absorption ratio:

A piece of tissue paper folded twice and kept on a small petri dish, to that 6 ml of water was poured. A tablet was put on the tissue paper allowed to wet completely. The wetted tablet was then weighed. Water absorption ration R was calculated using following equation.

$$R = \frac{100(W_f - W_g)}{W_g}$$

Where,

W_f = weight of tablet after water absorption.

W_g = weight of tablet before water absorption.

***In – vitro* disintegration time:**

Disintegration time for FDTs was performed using USP disintegration apparatus pH 7.2 phosphate buffer. The volume of medium was 900 ml and temperature was 37 ± 0.2^{0}C. The time in second taken for complete disintegration of the tablet with no palatable mass present in the apparatus was measured [14].

***In – vitro* dissolution studies:**

The *in- vitro* dissolution rate study of ibuprofen fast dissolving tablets were performed using 8 stage dissolution test apparatus (Electrolab TDT-08L) fitted with paddles (50 rpm) at 37 ± 0.5^{0}C, using 7.2 phosphate buffer of 900 ml as a dissolution media. At the predetermined time intervals, 5 ml samples were withdrawn, filtered through 0.45µ membrane filter, diluted and assayed at 221 nm using a Analytical technology T360 UV/Visible Double beam spectrophotometer. Cumulative percentage release was determined using standard absorbance from the calibration curve. All the dissolution experiments were performed in triplicate (n = 3).

RESULTS AND DISCUSSION

The starch succinate prepared was found to be fine, free flowing crystalline powder. The physical and micromeritic properties of the starch succinate are compiled in table 2. It was insoluble in aqueous solvents and insoluble in organic solvents tested (methanol, petroleum ether, dichloromethane, and chloroform) the pH of 0.1% aqueous dispersion was 3.98.

Starch succinate exhibited good swelling in water. The swelling index was found to be 62.4%. All micrometric properties indicated good flow and compressibility needed for solid dosage from manufacturing. The density of starch succinate was found to be 0.481g/cc The angle of repose and compressibility index showed good flow properties of starch succinate. The FTIR spectrum of potato starch and starch succinate is shown in Fig: 1 and 2. The presence of peaks absorption at 1204.42cm^{-1} characteristic peak of ester, so from FTIR studies it was concluded that starch succinate (ester) was formed when starch was allowed to react with tartaric acid. The X-ray diffraction pattern (Fig: 3) of starch succinate showed characteristic peaks, which indicates that the structure is completely crystalline. The disappearance of pink color in the ester test confirmed the presence of ester, i.e., starch succinate. As the starch succinate was crystalline powder and it had got all the characteristic of superdisintegrants it was concluded that starch succinate can be used as novel superdisintegrant in the formulation of fast dissolving tablets.

Table: 2. Physical and micromeritics properties of the starch succinate prepared

Parameters	Observation
Solubility	Freely soluble in acetone. It dissolves in dilute solutions of alkali hydroxides and carbonates.
pH (1% w/v aqueous dispersion)	3.98
Melting point	Charred at 80ºC
Viscosity(1%w/v aqueous dispersion)	1.60 cps
Swelling index	62.4%
Gelling property	No gelling and the swollen particles of starch succinate separated from water. Where as in the case of starch, it was gelatinized and formed gel.
Moisture absorption	4.1%
Particle size	250 µm (80/120mesh)
Density	0.481 g/cc
Bulk density	0.495 g/cc
Angle of repose	25.2º
Compressibility index	9.17%

*SD Standard Deviation from mean. n=3

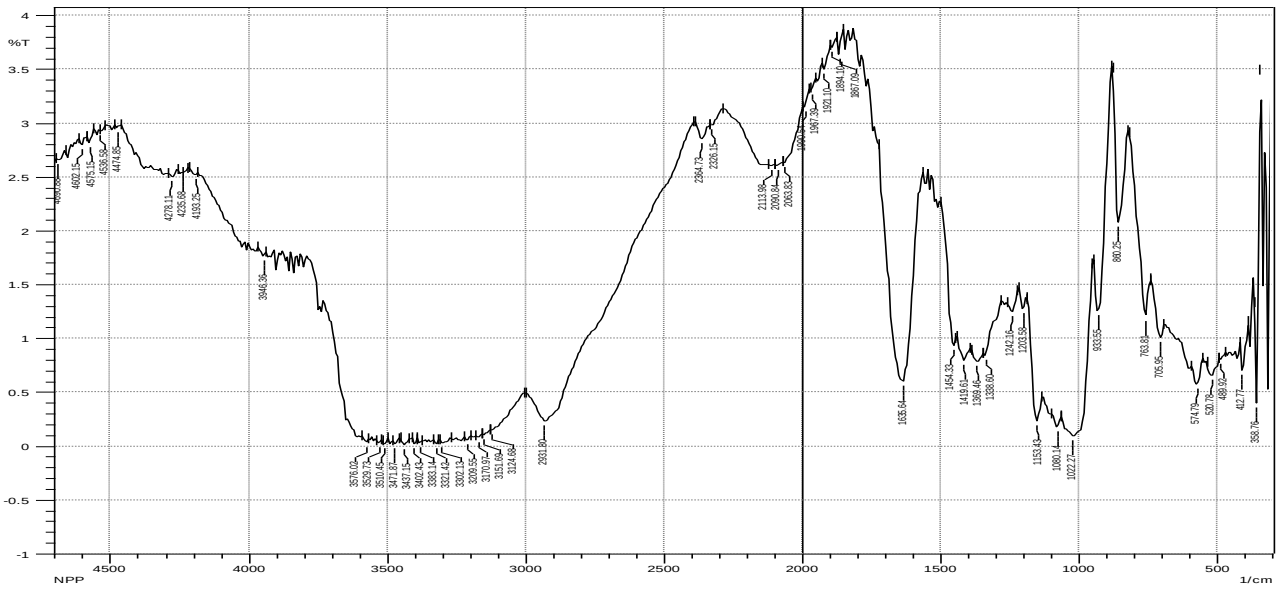

Figure 1: Fourier transform infrared spectra of potato starch.

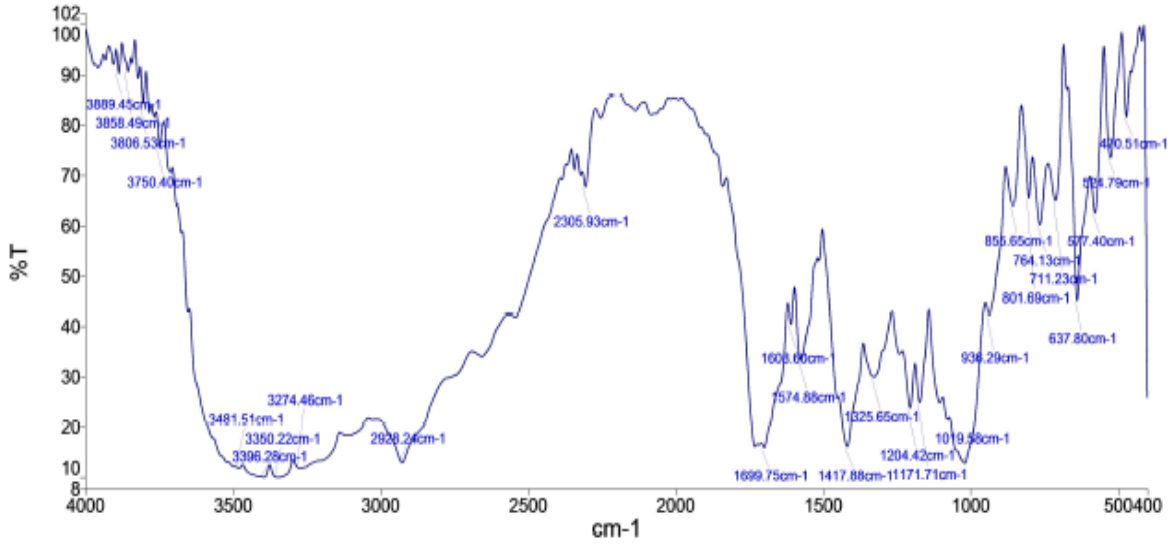

Figure 2: Fourier transform infra red spectra of starch succinate

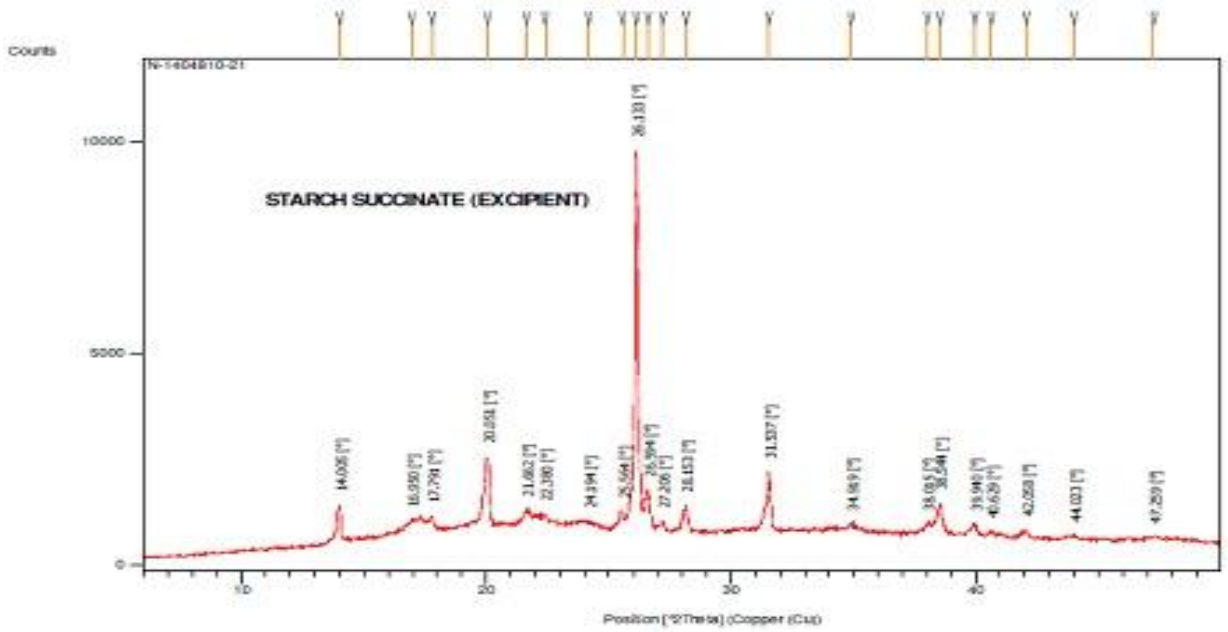

Figure 3: X-Ray diffraction pattern of starch succinate

The X-ray diffraction pattern of starch succinate showed no charactersistic peaks, which indicates that structure is amorphous shown in Fig.3. The compatibility of starch succinate with the selected drug (Ibuprofen) was evaluated by DSC, FTIR studies and TLC studies.. The DSC thermograms of ibuprofen and ibuprofen – starch succinate are shown in Fig.4 and 5. The DSC thermograms of ibuprofen and ibuprofen – starch succinate exhibited exothermic peaks at 79.77ºC and 79.02ºC respectively. These melting peaks of ibuprofen and ibuprofen – starch succinate are nearer to the melting points of ibuprofen (75-78^{0}C). The peaks observed in the DSC thermograms of ibuprofen and ibuprofen – starch succinate mixtures correspond to the melting points of the respective drug indicating no interactions between the selected drug and starch succinate polymer. The DSC study, thus, indicated no interaction between starch tartrate and selected drug.

The FTIR spectra of ibuprofen and ibuprofen – starch succinate are shown in Figs.6 and 7. The characteristic FTIR bands of ibuprofen at 2955.62 cm^{-1} (COOH), 1508.54 cm^{-1} (C=C), 1720.83 cm^{-1} (C=O) were all observed in the FTIR spectra of both IB and IB- SS. These FTIR spectral observations also indicated no interaction between starch succinate and the drug selected.

In the TLC study, single spots were observed in the case of pure drugs as well as their mixtures with starch succinate are shown in Fig 8. The close agreement of the R_f values of the drugs and their mixtures with starch succinate (Table 3) indicated no interaction between the drug and starch succinate.

Thus the result of DSC, FTIR and TLC indicated no interaction between the selected drug and starch succinate, the new superdisintegrant. Hence, starch succinate could be used as a superdisintegrant in the design of fast dissolving tablets of the selected drug.

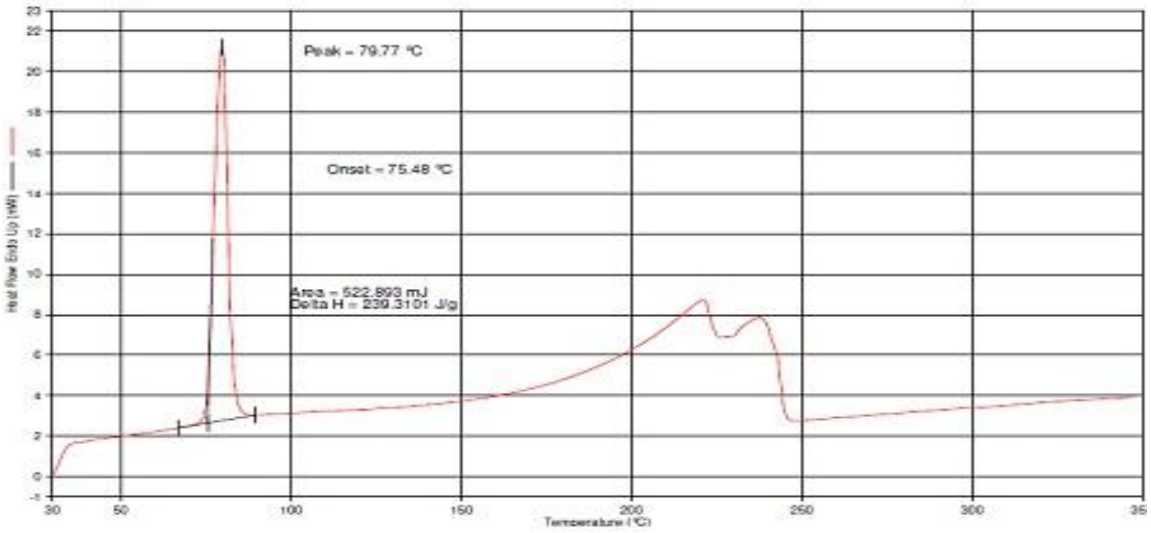

Figure 4: DSC Thermogram of ibuprofen pure drug

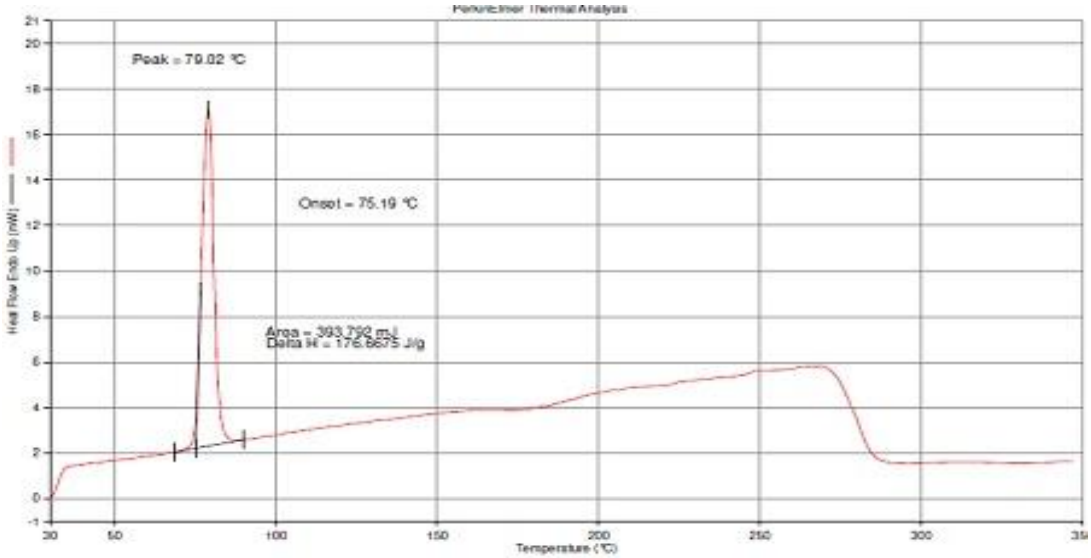

Figure 5: DSC Thermo gram of ibuprofen with starch succinate

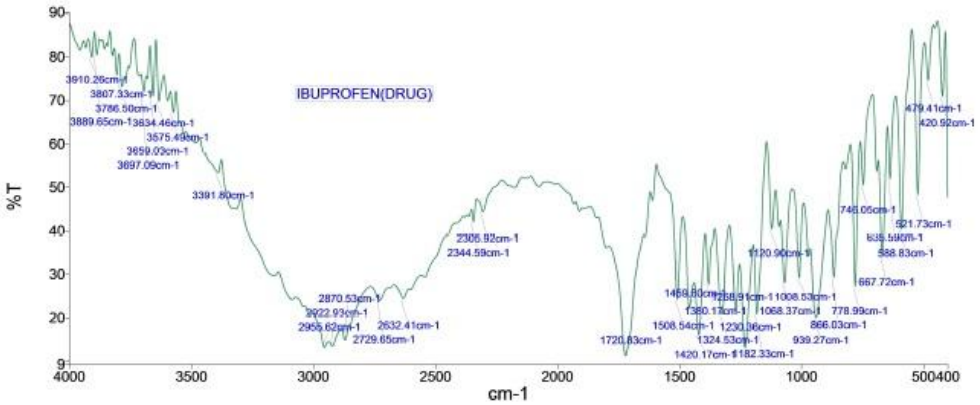

Figure 6: FTIR spectra of ibuprofen

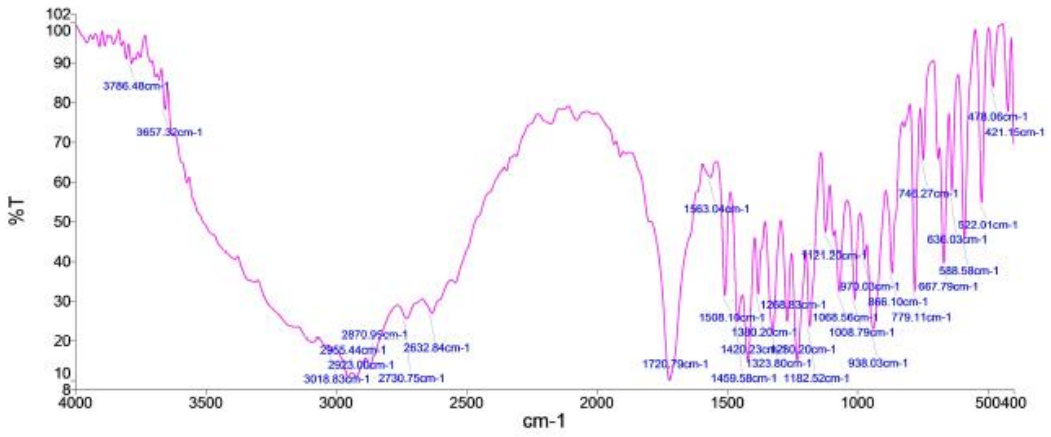

Figure 7: FTIR Spectra of ibuprofen with starch succinate

Table: 3 R_f Values of Selected Drugs and their Mixtures (1:1) with starch succinate

S. No	Product	R_f Value
1.	Ibuprofen	0.230
2.	Ibuprofen-Starch succinate	0.227

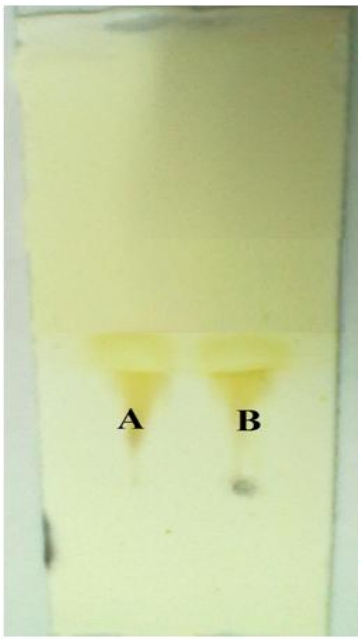

Figure 8: TLC plate showing (A) Ibuprofen pure drug (B) Ibuprofen and Starch succinate

Evaluation of tablets

Hardness

Hardness of tablets from all batches was found to be in the range of 3.6±0.03 kg/cm^2 to 4.0± 0.04 kg/cm^2. All tablets were found to be strong enough to withstand the handling and storage conditions of without getting broken.

Friability

All the tablets shown acceptable friability as none of the tested batches exhibited percentage friability that exceeded 1%. As per IP, % friability of less than 1% is an indication of good mechanical resistance of the tablets. Percent friability of all batches were found in the range of 0.12±0.013%-0.15±0.012%. Thus, it was concluded that tablets could withstand the pressure, mechanical shocks during handling, transportation, storage and manufacturing processes.

Drug content

Drug content of all the formulation batches was found to be between 198.02±0.57 to 199.56±0.55. Hence, it can be decided that all the formulations are having an accurate amount of drug distributed uniformly in powder mass and followed acceptable limits as per IP in range of 85 to 115 % of average content table 4 [15].

Disintegration studies

In vitro disintegration time was performed by the USP dissolution apparatus. The disintegration rate has a correlation with water absorption capacity of disintegrate and the *in vitro* disintegration time was found between 15±02 to 132±03s. The outcomes were tabulated and data demonstrated in table 4. The disintegration times of all the formulation were less than 132 s. It was found that the formulation F8 has least disintegration time 15s when compared to other formulations. The order of a disintegration time in fast dissolving tablets was found to be F8<F6<F2=F7<F4<F5<F3<F1. The order of disintegration time may be due to the interaction and main effects of the super disintegrants used in the fast dissolving tablets.

Water absorption ratio and wetting time

The water absorption ratio was in between 31.4±0.01 - 68.0±0.04. The wetting time found between 15±0.11 - 100±0.51s. The outcomes were tabulated and data demonstrated in table 3 and Fig. 9 and 9a. It was found that the formulation F8 containing 10 % starch succinate, 10 % croscarmellose sodium, 10 % crospovidone showed less wetting time i.e. 15±0.11 s as compared to other formulations.

***In vitro* dissolution studies**

Dissolution rate depends on the wetting time of the disintegrants, among all the formulations F8 has less wetting time and has greater dissolution rate which give the other conformance test for correct selection of desirable. *In vitro* dissolution studies of all the formulation were performed and depicted in fig.10 and 10a. In all formulations F8 formulation was selected as the promising formulation containing 10 % starch succinate, 10 % Croscarmellose sodium, 10 % Crospovidone with 99.81± 0.22% release in 5

min which may be due to the interaction effect between the three super disintegrants i.e., 10 % starch succinate, 10 % Croscarmellose sodium, 10 % Crospovidone. The dissolution parameters of the formulation from (F1–F8) which were made by wet granulation method were shown in the table: 5. In all these cases the PD_5 (percent dissolved in 5 minute) was more in F8 which consists at 10 % starch succinate, 10 % Croscarmellose sodium, 10 % Crospovidone. The same was in the case of DE_5 % (dissolution efficiency in 5 min). The PD_5& DE_5 % revels that 10 % starch succinate, 10 % Croscarmellose sodium, 10 % Crospovidone was effective. When the formulations were made by direct compression using these superdisintegrants. The number of folds are in the order of F3<F5<F2<F7<F4<F6<F8 in DE_5% were given to the table 5. From the results, it was concluded that starch succinate (new superdisintegrant) could be used as a super disintegrant in the formulation of fast dissolving tablets of ibuprofen. To assess the individual and combined effects of the three factors involved, fast dissolving tablets were formulated employing selected combinations of the factors as per 2^3-factorial design. The fast dissolving tablets and the release parameters (percent drug released in 5 min) of the fast dissolving formulated were analyzed as per ANOVA of 2^3-factorial design. ANOVA of fast disintegrating time (table 6), ANOVA of dissolution efficiency in 5 min (table 7) indicated that the individual effects of starch succinate (A), crospovidone (B) and croscarmellose sodium (C), as well as the combined effects of AB, AC, BC and ABC factors, were significant (P<0.05) on disintegration time and dissolution efficiency in 5 min of ibuprofen fast dissolving tablets.

Fast dissolving tablets formulated employing 10 % starch succinate, 10 % Croscarmellose sodium, 10 % Crospovidone as super disintegrants exhibited in disintegration and dissolution efficiency in 5 min. Formulation F8 gave release of 99.81in 5 min fulfilling the official specification, based on disintegration time and dissolution efficiency in 5 min. Formulation F8 is considered as a good fast dissolving tablet formulations of ibuprofen which was found to better than the ibuprofen fast dissolving tablets formulated by Sai Kishore *et al* [15].

Table.4: Physical Properties: Hardness, Friability Drug Content of ibuprofen fast dissolving tablets prepared.

Formulation	Hardness (Kg/Cm^2)n ± S.D	Friability (%) n ± S.D	Drug Content (Mg/Tab) n ± S.D	Disintegration Time (Sec) n ± S.D	Water Absorption Ratio (%) n ± S.D
F1	3.9± 0.01	0.12±0.013	198.89±0.71	132±03	42.9±0.52
F2	3.6± 0.03	0.13±0.015	199.10±0.79	32±02	50.0±0.55
F3	4.0± 0.01	0.14±0.012	198.82±0.63	50±02	48.9±0.01
F4	3.8± 0.04	0.12±0.014	199.56±0.55	42±03	51.5±0.21
F5	3.7± 0.03	0.14±0.014	199.13±0.56	45±04	52.9±0.52
F6	3.9± 0.01	0.15±0.012	199.21±0.21	30±02	58.0±0.02
F7	3.7± 0.02	0.14±0.014	198.02±0.57	32±03	31.4±0.01
F8	4.0± 0.04	0.12±0.013	199.32±0.11	15±02	68.0±0.04

*SD Standard Deviation from mean, n=3

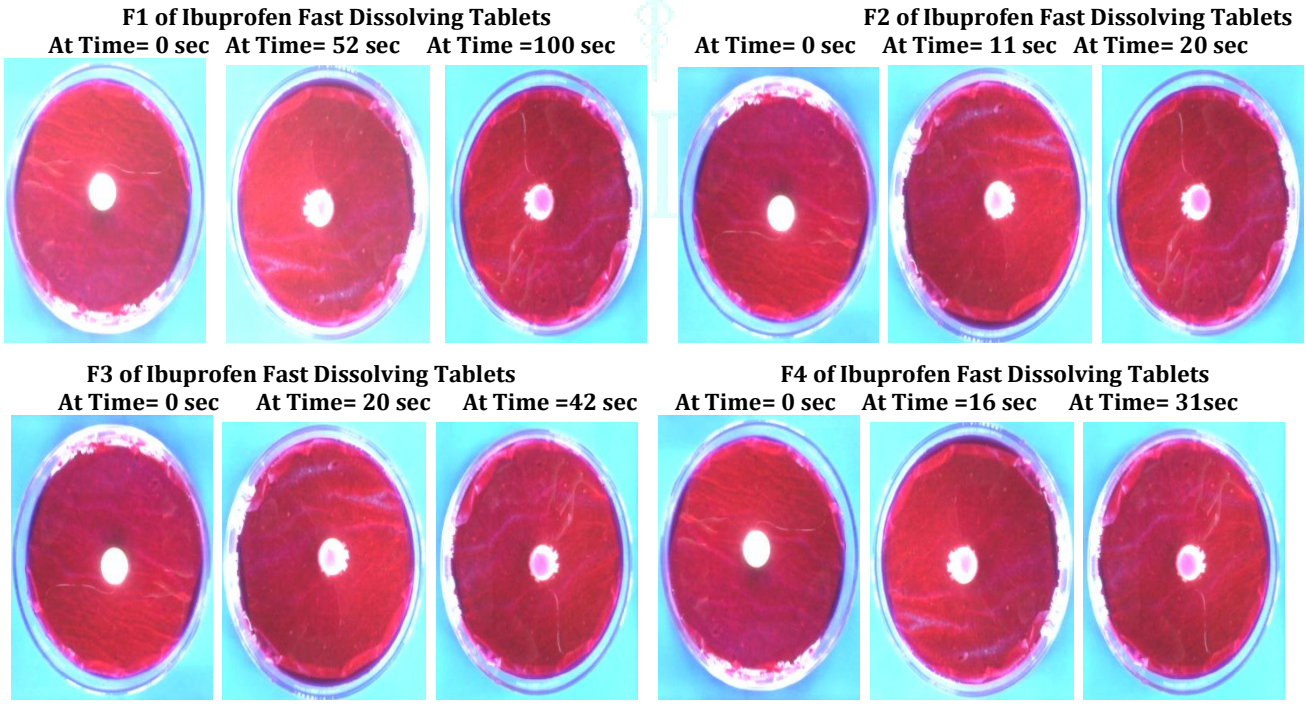

Figure 9: Ibuprofen fast dissolving tablets prepared employing starch succinate

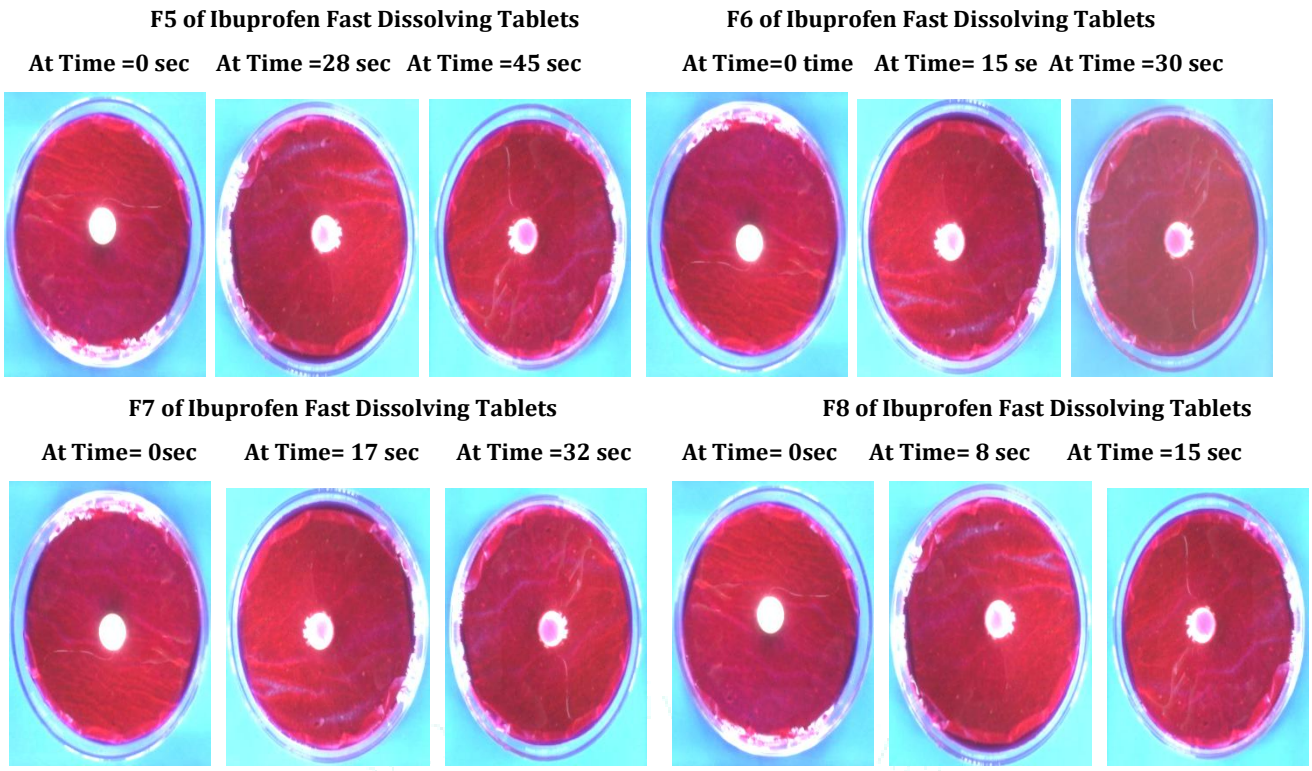

Figure 9 (a): Ibuprofen Fast Dissolving Tablets Prepared Employing Starch Succinate

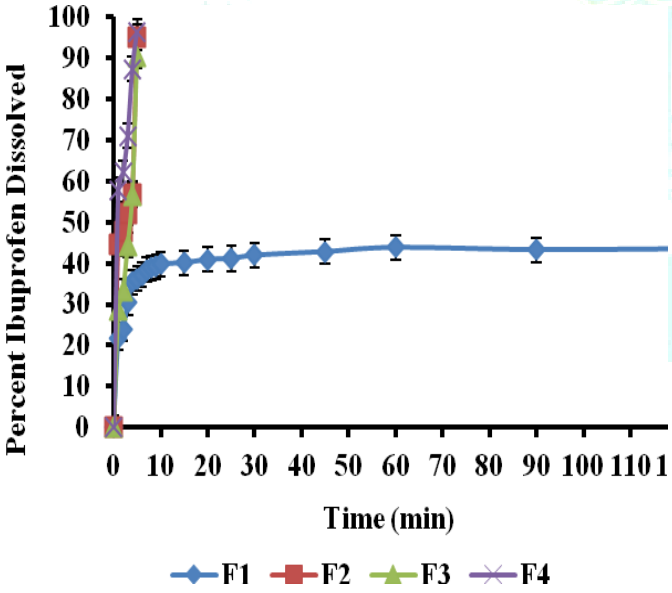

Figure 10: Dissolution profiles of ibuprofen fast dissolving tablets prepared employing starch succinate

(F1- F4) (n=3, mean±SD)

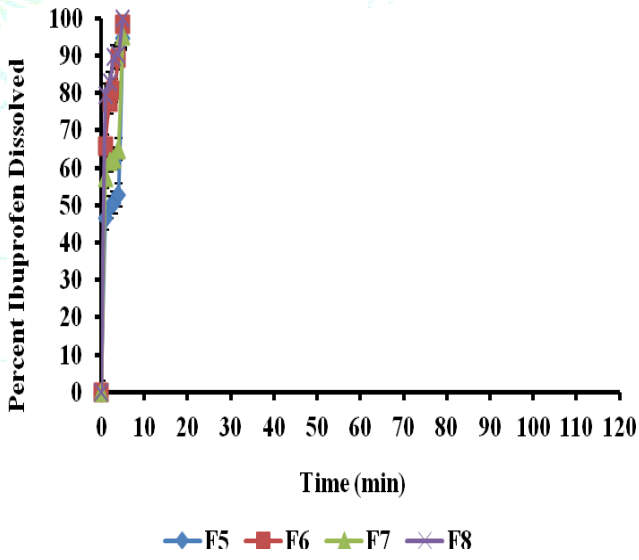

Figure 10a: Dissolution profiles of ibuprofen fast dissolving tablets prepared employing starch succinate

(F5- F8) (n=3, mean±SD)

Table 5: Dissolution parameters of ibuprofen fast dissolving tablets formulated employing starch succinate and other known superdisintegrants

Parameters	F1	F2	F3	F4	F5	F6	F7	F8
PD_5	36.27	95.02	90.48	96.40	94.67	98.42	95.12	99.81
DE_5 (%)	25	47	38	66	46	72	50	80
Increase in DE_5 (%) No of Folds	--	1.88	1.52	2.64	1.84	2.88	2	3.2
K (min^{-1})	0.115	0.156	0.180	1.120	0.178	0.594	0.621	0.121
Increase in K (min^{-1}) No of Folds	--	1.356	1.565	9.739	1.547	5.165	5.40	1.052

*SD Standard Deviation from mean, n=3, PD5-Percent dissolved in 5 min., DE5%-Dissolution efficiency in 5 min., K1 =First Order Rate Constant

Table 6 ANOVA of disintegrating times in 5 min of ibuprofen fast dissolving tablets formulated employing starch succinate

Source of Variation	d. f	S.S	M.S.S	Variance ratio	Result
Replicates	2	19.09	9.545	11.51	P > 0.05
Treatments	7	450.14	64.28	43.8	P < 0.05
Starch succinate (A)	1	595.5	595.5	81.5	P < 0.05
Croscaramellose(B)	1	992.66	992.66	97.4	P < 0.05
Starch succinate X Croscaramellose sodium (AB)	1	392.66	392.66	67.9	P < 0.05
Crospovidone (C)	1	592.8	592.8	69.9	P < 0.05
Starch succinate X Crospovidone (AC)	1	308.2	308.2	37.5	P < 0.05
Croscarmellose sodium X Crospovidone (BC)	1	126.1	126.1	21.71	P < 0.05
Starch succinate X Croscarmellose sodium X Crospovidone (ABC)	1	252.8	252.8	41.61	P < 0.05
Error	14	11.61	0.829	--	--
Total	23	--	--	--	--

*SD Standard Deviation from mean, n=3, P<0.05 indicate significance; p>0.05 indicate non-significance, d. f–Degree of Freedom
*S. S–Sum of Square *M. S. S–Mean Sum of Squares, ANOVA= Analysis of Variance

Table 7 ANOVA of dissolution efficiency in 5 min of ibuprofen fast dissolving tablets formulated employing starch succinate

Source of Variation	d. f	S.S	M.S.S	Variance ratio	Result
Replicates	2	26.08	13.04	27.33	P > 0.05
Treatments	7	855.2	79.54	53.0	P < 0.05
Starch succinate (A)	1	413.3	413.3	67.4	P < 0.05
Croscaramellose(B)	1	715.4	715.4	99.0	P < 0.05
Starch succinate X Croscaramellose sodium (AB)	1	478.8	478.8	38.5	P < 0.05
Crospovidone (C)	1	820.4	820.4	15.55	P < 0.05
Starch succinate X Crospovidone (AC)	1	150.4	150.4	31.53	P < 0.05
Croscarmellose sodium X Crospovidone (BC)	1	135.3	135.3	3.79	P < 0.05
Starch succinate X Croscarmellose sodium X Crospovidone (ABC)	1	478.8	478.8	38.46	P < 0.05
Error	14	6.68	--	--	--
Total	23	--	--	--	--

*SD Standard Deviation from mean, n=3, P<0.05 indicate significance; p>0.05 indicate non-significance, d. f–Degree of Freedom
*S. S–Sum of Square *M. S. S–Mean Sum of Squares, ANOVA= Analysis of Variance

CONCLUSION

Starch succinate is an efficient superdisintegrant for fast dissolving tablets. The disintegration and dissolution efficiency of the fast dissolving tablets of ibuprofen was good and depended on the concentration of superdisintegrant employed i.e., 10 % starch succinate, 10 % Croscarmellose sodium, 10 % Crospovidone. The formulated fast dissolving tablets of ibuprofen employing starch succinate, croscarmellose sodium, and crospovidone exhibited good dissolution efficiency in 5 min which can be used for the fast therapeutic action of ibuprofen.

Overall, Starch succinate was found to be a super-disintegrant in the formulation of fast dissolving tablets to provide immediate release of the poorly soluble drugs.

Abbreviations

FTIR - Fourier transform infrared spectra

DSC - Differential scanning calorimetry

ANOVA – Analysis of variance

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